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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/479,997	06/07/95	ENGELHARDT	D ENZ-5 (D6) (C2)

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HM31/0929

ART UNIT EXAMINER PAPER NUMBER

DATE MAILED: 1634

19

09/29/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No. 08/479,997	Applicant(s) Engelhardt et al.
Examiner Scott W. Houtteman	Group Art Unit 1634

Responsive to communication(s) filed on Jul 9, 1998

This action is FINAL.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

Claim(s) 310-372 and 405-453 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

Claim(s) 310-372 and 405-453 is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- Notice of References Cited, PTO-892
- Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- Interview Summary, PTO-413
- Notice of Draftsperson's Patent Drawing Review, PTO-948
- Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to:

Art Unit: 1634

Examiner: Scott Houtteman

2. Applicant's response, filed 7/9/98, has been carefully considered with the following effect:
All objections and rejections of Office action mailed 1/6/98, have been maintained.
3. Claims 310-372 and 405-453 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

Applicant's argument is essentially that (1) no prima facie case has been made and (2) that the improper legal standard has been used because of the use of the word "explicit." These arguments are not persuasive. A prima facie case has been established by supplying reasons that a skilled artisan would not have reasonably expected this specification to put the artisan in possession of the invention as now claimed.

With respect to the adjective "explicit," which was used in the body of the rejection. This word is synonymous with definite, distinct, precise or specific. Any and all of these words can be used to explain a rejection. The legal standard was summarized in the final paragraph, as is customary, and is the same as the standard cited in the argument, that the specification put the

artisan in possession of the invention as now claimed. See Office action mailed 1/6/98, page 3, second paragraph from the bottom. This summary paragraph was not addressed in the argument.

4.

Claims 310-372 and 405-453 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record.

Applicant argues that example V on page 57 of the specification describes "biotinylated poly-L-lysine is coupled to a terminal oxygen of the phosphate moiety or to a terminal phosphorus."

This argument is not persuasive. Example V on page 57 describes "Biotin and polybiotinylated poly-L-lysine" attached to "oligoribonucleotides" not a generalized "sig" moiety attached to the terminal oxygen or phosphate moiety. The specification says nothing about why specific detectable labels, biotin and polybiotinylated poly-L-lysine, are necessarily a description of the generic "SIG" moiety. Also, the specification says nothing about where these labels are attached to the oligoribonucleotides. The argument does not address why the specific attachment sites, terminal oxygen or phosphate moiety, are "necessarily" and "inherently" described by this generic teaching.

5. Claims 310-372 and 405-453 are rejected under 35 U.S.C. § 103 for being unpatentable over Gohlke et al., US Patent 4,378,458, 3/1983, filed 3/1981 (Gohlke) in view of Sodja et al., Nucleic Acids res., 5(2):385-401, 1978 (Sodja) and further in view of applicant's admissions.

6. Applicant argues briefly, that the Gohlke substrate "cannot in any way be polymerized or incorporated into an oligo- or polynucleotide or other polymeric composition." This argument is not persuasive. There is no need to polymerize the mononucleotide after adding the label. One need only polymerize the mononucleotide before adding the label or simply add the label to a preexisting polynucleotide.

Applicant argues, on a "technicality," that the Sodja open sugar ring means that "the resulting product is no longer a nucleotide." This argument ignores the fact that even if the terminal base of an oligonucleotide were altered, the resulting product, a terminal base/label complex, still reads on the claimed invention. Sodja teaches the attachment of the label to an oligonucleotide, not a mononucleotide. Thus, the Sodja product, a "SIG" moiety, is still attached to an oligonucleotide by the phosphate moiety. The terminal base/label complex falls within the "SIG" definition and this complex is attached to the penultimate base on the oligonucleotide by the phosphate moiety. Thus the resulting product still suggested the claimed product.

More importantly, applicant's "technicality" argument completely ignores the fact that the Sodja product is used in hybridization experiments. It matters little whether "the resulting product [the terminal base] is no longer a nucleotide" because the Sodja product retains all functional properties of a nucleic acid. Thus, practically speaking, the Sodja product is a

phosphate labeled oligonucleotide whether or not some of the base residues have some trivial altered structure.

7. Perhaps most importantly of all, applicants arguments to the 35 U.S.C. § 112, first paragraph rejections have provided strong evidence of obviousness and vice-versa. This has been pointed out in a previous Office action but has not been addressed in applicants response. Thus, it appears that the arguments concede that, on these grounds at least, rejections are proper.

It is important that the arguments for patentability explain, in view of the thin disclosure about "SIG-Phosphate" reactions, that the prior art supplied by applicant can buttress the specification--providing needed evidence that the thin "SIG Phosphate" disclosure "describes" the detailed invention now claimed--but that this same prior art references do not render the claims obvious.

Unfortunately, applicant must also explain why the argument's criticisms of the obviousness rejection, specifically the teachings of the prior art supplied in the obviousness rejection, are not evidence of the specification's lack of enablement and the lack of descriptive support. After all, the specification lacks much more detail than supplied by the prior art teachings in the obviousness rejection. Furthermore, the specification is held to a higher standard than the teachings of the prior art supplied in an obviousness rejection. As stated in a previous office action:

35 U.S.C. § 112 provides that, in return for the grant of monopoly, the specification must enable one skilled in the art to "make and use" the invention without "undue experimentation" whereas 35 U.S.C. § 103 makes no such requirement. Thus, a teaching

of how to use a compound can be entirely adequate to render a claim obvious but, at the same time, entirely inadequate to support the allowance of such a claim.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

9. This application is subject to the provisions of Public Law 103-465, effective June 8, 1995. Accordingly, since this application has been pending for at least two years as of June 8, 1995, taking into account any reference to an earlier filed application under 35 U.S.C. 120, 121 or 365(c), applicant, under 37 CFR 1.129(a), is entitled to have a first submission entered and considered on the merits if, prior to abandonment, the submission and the fee set forth in 37 CFR 1.17(r) are filed prior to the filing of an appeal brief under 37 CFR 1.192. Upon the timely filing of a first submission and the appropriate fee of \$770 for a large entity under 37 CFR 1.17(r), the finality of the previous Office action will be withdrawn. In view of 35 U.S.C. 132, no amendment considered as a result of payment of the fee set forth in 37 CFR 1.17(r) may introduce new matter into the disclosure of the application.

If applicant has filed multiple proposed amendments which, when entered, would conflict with one another, specific instructions for entry or non-entry of each such amendment should be provided upon payment of any fee under 37 CFR 1.17(r).

10. Papers relating to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Art Unit 1809. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Art Unit 1809 Fax number is (703) 305-7401.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott Houtteman whose telephone number is (703) 308-3885. The examiner can normally be reached on Tuesday-Friday from 8:30 AM - 6:00 PM. The examiner can also be reached on alternate Mondays.

Serial No. 08/479,997
Art Unit 1809

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Scott Houtteman
September 28, 1998



**SCOTT W. HOUTTEMAN
PRIMARY EXAMINER**